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Letters to the Editor

Acute acalculous cholecystitis as a manifestation of ehrlichiosis

1. Introduction

Almost half of the total number of ehrlichiosis cases reported in New York State are from Suffolk County in Long Island, NY (New York State Department of Health, 2016). Ehrlichiosis in this region is caused by *Ehrlichia chaffeensis*, a tick-borne pathogen transmitted by *Amblyomma americanum*. The number of cases of ehrlichiosis in this county has increased significantly during the last decade, likely due to expansion of the population of *A. americanum* (Mixson et al., 2004). The clinical course is usually uncomplicated, however severe complications can occur.

2. Case report

A 57-year-old female from Long Island presented to the emergency department with a 4-day history of persistent high-grade fevers, rigors, right upper quadrant abdominal pain, and dry, nonproductive cough. She was lethargic but able to answer questions. She did not remember any recent tick bites but stated that she walked to the beach nearly every day near her home. On presentation, the patient was febrile to 39.2 °C, with blood pressure of 92/62 mmHg, heart rate of 114 beats per minute, and respiratory rate of 22 breaths/minute. Abdominal exam revealed a soft abdomen with right upper quadrant abdominal tenderness on palpation without rebound tenderness. Murphy's sign was positive. A faint erythematous rash was noted on her trunk. Mottling of the skin was noted on her lower extremities. Admission labs were significant for a metabolic acidosis with an anion gap of 16. Serum creatinine was 0.6 mg/dl. Liver function tests revealed total bilirubin 0.5 mg/dL, direct bilirubin < 0.2 mg/dL, ALT 260 U/L, AST 384 U/L, and alkaline phosphatase 101 U/L. Complete blood count revealed a leukocyte count of 2.36 × 10^3/μL with 19% bands, hemoglobin 12.7 g/dL, and platelet count of 74 × 10^3/μL. CT of the abdomen and pelvis without IV contrast showed hepatomegaly, a distended gallbladder with areas of possible wall thickening, and pericholecystic fluid tracking into the perihepatic region. A follow-up abdominal ultrasound demonstrated a dilated gallbladder, 5 cm in diameter, with areas of focal wall thickening with a sonographic positive Murphy's sign. The patient was diagnosed with acute cholecystitis. Due to her borderline hemodynamic status, she was admitted to the medical intensive care unit, started on intravenous antibiotics and underwent percutaneous cholecystostomy on hospital day 1. Doxycycline was given at a dose of 200 mg IV loading dose (6 h prior to the cholecystostomy) followed by 100 mg IV every 12 h, given empirically due to the suspicion for tick-borne illness. During the hospitalization, whole blood specimens that had been collected 3 days prior to admission and on the day of admission were reported by a reference laboratory as positive for *E. chaffeensis* DNA based on a real-time PCR assay. The patient's clinical status rapidly improved; however, she continued to have right upper abdominal pain and underwent laparoscopic cholecystectomy on hospital day 4. Examination of the gallbladder revealed acute and chronic cholecystitis without any evidence of stones. She was discharged on hospital day 6 and prescribed a 10-day course of doxycycline for treatment of *E. chaffeensis* infection, with subsequent full recovery. The gallbladder specimen obtained during surgery was sent to the Centers for Disease Control in Atlanta, GA for molecular studies. *E. chaffeensis* DNA was detected in a tissue extract using a real-time PCR assay that targeted the 16S rRNA gene. Immunohistochemistry (IHC) staining with a polyclonal antibody was negative for *Ehrlichia* spp. antigens. Microscopic examination revealed blood and lymphatic vessels throughout the submucosa and surrounding adventitia containing moderate numbers of mixed circulating inflammatory cells with predominance of lymphocytes, plasma cells, and prominent numbers of eosinophils, with extravasation and scattered infiltration of the submucosa. Mucosal epithelium was intact. No morulae were observed within circulating white blood cells, likely due to insensitivity of H&E staining; IHC may have been negative because the patient had received 5 days of doxycycline therapy prior to the cholecystectomy.

3. Discussion

We describe a case of human monocytic ehrlichiosis that presented with acute acalculous cholecystitis. It is possible that systemic infection with *E. chaffeensis* triggered infection-related recruitment of inflammatory cells to the gallbladder causing the cholecystitis, rather than localized infection of the gallbladder wall since the IHC was negative (the positive test for *E. chaffeensis* DNA does not necessarily indicate the presence of intact or viable organisms). Review of the literature is notable for two cases of ehrlichiosis that were associated with acute cholecystitis; however, the *Ehrlichia* etiology was not initially suspected and the patients had complicated clinical courses. One case involved a 63-year-old female who developed fever, abdominal pain, myalgia, and pancytopenia two days after removal of a tick. She was diagnosed with acute cholecystitis and underwent cholecystectomy on hospital day 2. Her postoperative course was complicated by extensive postoperative bleeding. She was diagnosed and treated for ehrlichiosis shortly after surgical intervention, but had a prolonged hospital course and was discharged on hospital day 28 (Centers for Disease Control and Prevention (CDC, 1996). Another case described a 51-year-old female from Jacksonville, FL, who sustained multiple tick bites while working in a wooded area and presented to the hospital two weeks later with lethargy, right upper quadrant pain, and elevated transaminase levels. She was diagnosed with acute cholecystitis and underwent cholecystectomy on hospital day 2. She developed acute respiratory distress syndrome and anuria postoperatively; IV doxycycline was started on hospital day 5 and she died on day 6. Serology performed on specimens from days 1 and 6 exhibited a diagnostic 4-fold rise in *E. chaffeensis* IgG titers (Paddock et al., 1997).

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4. Why should an emergency physician be aware of this?

Our case illustrates the importance of considering ehrlichiosis in the differential diagnosis of patients who present with sepsis, abdominal pain, and abnormal liver function tests, particularly in the summer months in endemic regions of the southeast, mid-Atlantic, and northeast United States. Severe infections due to human monocytic ehrlichiosis can present with clinical features similar to more common forms of acute cholecystitis and early surgical intervention without appropriate antibiotic therapy may lead to poor clinical outcomes.

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